REMARKS

Claims 1, 7-11, 32, 36 and 39 are pending in this application. Claims 18-20, 23, 24, 26, 28 and 29 are cancelled with this amendment. Claims 1 and 32 are amended herein. Support for the amendments to claims 1 and 32 can be found, for example, in priority document USSN 60/121,836 at page 4, lines 8-23; page 5, lines 20-27; and Figure 1, as well as the instant specification, *e.g.*, page 8, line 22 through page 9, line 20; page 10, lines 1-19; and Figures 1 and 4A. No new matter is added.

Rejections under 35 U.S.C. §112

Written Description

The Examiner has rejected claims 1, 7-11, 32, 36 and 39 for lack of written description. The Examiner alleged in paragraph 12 of the Office Action that, "the specification does not reasonably suggest that applicant was in possession of the immense genus of probes encompassed by the claimed device." Applicants traverse to the extent it is applied to the claims as amended.

The test for determining whether a claim fulfills the written description requirement is set forth in Amgen Inc. v. Hoechst Marion Roussel, Inc.[1]

> The purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not; the applicant for a patent is therefore required to "recount his invention in such detail that his future claims can be determined to be encompassed within his original creation." Satisfaction of this requirement is measured by the understanding of the ordinarily skilled artisan. ("The description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Compliance with the written description requirement is essentially a fact-based inquiry that will 'necessarily vary depending on the nature of the invention claimed'.

[1] 314 F.3d 1313 , 65 USPQ2d 1385, (Fed. Cir. 2003) (internal citations omitted)

An objective standard for determining compliance with written description is whether the disclosure of the application relied upon reasonably conveys to persons of ordinary skill in the art that the Applicant had possession of the claimed subject matter as of the date of the invention.[2,3]

The present rejection can be compared to the written description issue addressed by the Court in Amgen Inc. v. Hoechst Marion Roussel, Inc. and Transkaryotic Therapies, Inc., 314 F.3d 1313, 85 USPQ2d (BNA) 1385 (Fed. Cir. 2003) In this case, the accused infringer argued that the patentee's claims drawn to "vertebrate cells" in U.S. Patent No. 5,756,349 did not meet the written description provision of 35 U.S.C. §112, first paragraph because the patentee failed to sufficiently describe the use of all vertebrate cells but rather only disclosed CHO (hamster) and COS-1 (monkey) cells in the specification.[4] The patentee argued that there are only "minor differences" in applying the method of the disclosed examples to any vertebrate cells, but that those of ordinary skill in the art could "easily" figure out those differences in methodology. Id. The Court agreed and reasoned that the word "vertebrate" readily conveyed distinguishing information concerning identity such that one of ordinary skill in the art could "visualize or recognize the identity of the members of the genus. Id.

Similarly, Applicants submit that the claim term "capture probe" conveys distinguishing information that is readily recognized by one of ordinary skill in the art in the context of the claimed invention. As is disclosed in the specification, nucleic acid hybridization is well known in the art, and an artisan can readily design a capture probe that hybridizes to a desired target molecule.

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[2] *In re Kaslow*, 707 F.2d 1366 (Fed. Cir. 1983)
[3] *In re Gosteli*, 872 F.2d. 1008 (Fed. Cir. 1989)
[4] Amgen Inc. v. Hoechst Marion Roussel, Inc. and Transkaryotic Therapies, Inc., 314 F.3d 1313 (Fed. Cir. 2003)

Enablement

The Examiner has rejected claims 1, 7-11, 32, 36 and 39 for lack of enablement. The Examiner alleged in paragraph 20 of the Office Action that Applicants cannot enable the use of an invention that they do not possess. As asserted above, Applicants have shown that there is sufficient written description for the invention of claims 1, 7-11, 32, 36 and 39, and thus Applicants possess the invention. Thus, claims 1, 7-11, 32, 36 and 39 are enabled insofar as Applicants possess the invention.

The Examiner further asserts that it would require one of ordinary skill in the art to use undue experimentation to make or use the instant invention. *In re Wands* set forth a number of factors to determine whether a disclosure would require undue experimentation. These factors are listed below.

(1) The quantity of experimentation necessary

Applicants submit that the quantity of experimentation necessary to practice the invention of claims 1, 7-11, 32, 36 and 39 is small to none. As explained on page 24, lines 3-4 of the instant specification, the capture probe is merely complementary to a portion of the target nucleic acid. The same strategy is taught on page 28, lines 17-19 of the instant specification. The making of a complementary nucleic acid probe to a target nucleic acid molecule is well within the abilities of one of ordinary skill in the art. Factors affecting the stringency of hybridization of complementary nucleic acids are also well known in the art as demonstrated in U.S. Patent No. 5,200,313, explained above. Further the instant specification gives workable conditions for hybridization of complementary nucleic acids in Example 1 on pages 23-26 of the instant specification. Thus, little or no experimentation is required to make and use the purification device, or the kit in which it is contained, as presently claimed.

(2) The amount of direction or guidance presented

The Examiner alleged in paragraph 24 of the Office Action that the guidance provided in the instant specification is limited. Applicants respectfully disagree. Applicants submit that the instant specification gives sufficient direction and guidance to assemble and practice the invention with any capture probe that is complementary in sequence to any given target nucleic acid. The instant specification shows how to make the gel in the device of the instant invention from page 23, line 15 to page 24, line 23, with the capture probe polymerized in the gel. The instant specification shows conditions used to capture a target nucleic acid molecule from page 25, line 14 to page 26, line 27.

(3) The presence of working examples.

In the instant application, Examples 1 and 2, on pages 23-29 show three working examples of capture oligos and hybridization conditions for using them.

(4) The nature of the invention.

The Examiner alleged in paragraph 24 of the Office Action that the nature of the art was unpredictable. Applicants respectfully disagree with the Examiner. The invention is drawn to a device and methods of using the device, wherein the device comprises capture oligos in a gel used to isolate target nucleic acid molecules. The specification discloses workable hybridization conditions selected from many known in the art. MPEP 2164.03 states:

> The scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required. A single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements. *In re Vickers*, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); *In re Cook*, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971). However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving

> unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work.

Unlike the chemical processes disclosed in *In re Fisher* (a claim to a preparation of adrenocorticotrophic hormone (ACTH) containing at least 1 International Unit of ACTH was not enabled by a specification which only disclosed preparations containing 1-2.2 International Units of ACTH) the capture oligos of the instant application involve predictable factors, *i.e.* complementarity and hybridization conditions well known in the art. Applicants are not required to supply every operable species required, especially in an art that is so well known. The Examiner also asserts that one of ordinary skill in the art would be able to make the probes of the instant invention. *See* the Office Action at paragraph 13. Because of this, the requirement for guidance in the invention of the instant application is low, but Applicants submit that this instant specification gives more than sufficient guidance for one of ordinary skill in the art to practice the invention.

(5) The state of the prior art.

Applicants submit that while the prior art does not disclose the invention of claims 1 and 32, the prior does show that hybridization of complementary nucleic acid molecules is well known. The Examiner alleged in the Office Action that the factors discussed in U.S. Patent No. 5,200,313 introduce complications that would cause undue experimentation to use the instant invention, because the '313 patent discloses factors that affect the extent and specificity of hybridization. *See* column 12, lines 8-46 of the '313 patent. However, the '313 patent asserts that these factors are "known in the art". *See* column 11, line 58 of the '313 patent. The '313 patent also states in

column 4, lines 50-56, "As is now well known in the art, contact of a first single stranded nucleic acid, either DNA or RNA, which comprises a base sequence sufficiently complementary to a second single stranded nucleic acid under appropriate solution conditions, will result in the formation of DNA.DNA, DNA.RNA, or RNA.RNA hybrids, as the case may be." (Emphasis added). Applicant submits that as of the filing date of the '313 patent on April 25, 1988, well before the filing date of the instant application, the hybridization of single stranded nucleic acids under appropriate solution conditions was well known in the art.

(6) The relative skill of those in the art

Applicants submit that the relative skill of those in the art is high. Generally, one of ordinary skill working on a biotechnology device would be the Ph.D. level. One of such skill would be well aware of the teachings in the art regarding nucleic acid molecule hybridization as exemplified above under subheading (5).

(7) The predictability of the art.

Applicants submit, as explained above, the hybridization of nucleic acid molecules and the appropriate conditions under which to hybridize them is well known in the art.

(8) The breadth of the claims.

The claims generally are drawn to a specific device used for the rapid isolation of a target nucleic acid molecule. The device or kit claimed requires a region with an electrophoretic medium copolymerized with a capture probe. The specification gives specific methods and conditions used with specific copolymerized capture probes. As in *In re Wands* at 740, the Applicants, "carried out

the procedure three times and [were] successful each time..." showing that "the amount of effort needed...is not excessive." Thus, Applicants submit that undue experimentation is not necessary to practice the claimed invention. Furthermore, claims 1 and 32 have been limited to require formation of a hybridization complex between the target nucleic acid and an immobilized capture probe. Thus, any embodiments that do not achieve a hybridization complex between the target nucleic acid and an immobilized capture probe are expressly disclaimed.

The Examiner further alleges that claims 1, 7-11, 32, 36 and 39 lack enablement in light of the technical problems shown in U.S. Patent Publication 2003/0133846 and 2002/0090641. Applicants traverse. *See* Office Action, paragraphs 21-23.

Applicants submit that the technical "problems" presented in the "Background of the Invention" section of the '846 publication are merely inconveniences, and do not render many of the techniques disclosed the Background of the '846 publication non-functional, and certainly do not render the device of the instant invention non-functional. For example, the techniques taught on paragraph 14 of the '846 publication lists "disadvantages" as being "i) the use of an impermeable membrane in the lower chamber results in dilution of the sample, thus requiring further concentration, ii) because the sample is contaminated with the electrophoretic buffer, an additional step (*e.g.* dialysis) is required to remove such contaminants." First, in Examples 1 and 2 of the instant invention, these technical disadvantages did not occur. Second, if they did, there would be techniques known in the art to further purify or condense samples prepared by the device and kit of the instant invention.

Further, this more specific treatment of the prior art electroelution device and procedure in paragraph 14 of the '846 application belies the statement quoted by the Examiner that, "Whereas electrophoretic separation of macromolecules is an established technique, the elution of

macromolecules from the gel has hitherto represented a difficult and generally non-reproducible procedure." Office Action, paragraph 22. There is no evidence that the procedure of paragraph 14 of the '846 application was difficult or generally non-reproducible. Indeed, a patent was granted on this device, as were the devices disclosed in paragraphs 11, 12, 13 and 15, all disclosing devices for elution of macromolecules from a gel. Applicant presumes that the Patent Office must have found the electroelution inventions of these patents enabled. While no method is totally without technical problems, the existence of technical problems does not render a claimed invention non-enabled. The standard is undue experimentation, and as reasoned in the *Wands* analysis above, undue experimentation is not necessary.

Applicants also note, that these paragraphs, being found in the Background of the Invention of an application for patent will be presented in a way most favorable to the patentability of the device sought to be patented in that application. Therefore, the drafters of this application had the incentive to denigrate the electroelution methods of the prior art to separate their own invention from it, thereby skewing the presented perspective of the operability of these methods.

Further, none of the allegedly "difficult or generally non-reproducible" procedures disclosed by the '846 publication are the procedures used for electroelution in the instant application. As shown in the instant specification, the electroelution methods of the instant application are not difficult and are generally reproducible. Therefore, Applicants submit that there are no relevant technical problems put forth in the '846 publication, and the claimed invention is enabled in light of the '846 publication.

Applicants also submit that the contamination problems alleged in paragraph 9 of the '641 publication are solved by the device and kit of the instant invention. Paragraph 9 of the '641 describes the problem of diffusion in the electrophoresis step of nucleic acid molecules when they

are separated by size. The '641 publication suggests the solution of this problem is the use of specific nucleic acid probes, and then heating the area with the probe annealed to the target nucleic acid molecule to release the target nucleic acid molecule without contamination of other target nucleic acid molecules. *See* paragraph 9 of the '641 publication. This is the same method employed in the instant invention. *See* Examples 3 and 4 on pages 29-30 of the instant specification. Therefore, the '641 application suggests that there are technical problems that are solved by the device and kit of the instant invention. Applicant submits that the technical problem introduced by the '641 publication is solved by the claimed invention, and thus the claims are enabled in light of the '641 publication.

Rejections under 35 USC 112, second paragraph

The Examiner has rejected claims 1, 7-11, 32, 36 and 39 as being incomplete for omitting the means to effect separation/purification of the nucleic acids of interest, *e.g.* an electrophoretic means. Applicants have amended claims 1 and 32 to require electrodes for generating an electrical field in the electrophoretic medium such that, when an electrical current is applied to the electrodes the target nucleic acid in the test sample moves from the receptacle to the electrophoretic medium and forms a hybridization complex with the immobilized capture probe, allowing molecules other than the target nucleic acid to migrate from the electrophoretic medium to the collection chamber. Figures 1, 2, and 4A describe how to effectuate purification of the target nucleic acid by applying an electric field to the device of the claimed invention.

Therefore, Applicants submit that claims 1, 7-11, 32, 36 and 39 are definite and this rejection should be withdrawn.

The Examiner has also rejected claims 1, 7-11, 32, 36 and 39 as being incomplete for

omitting essential structural cooperative relationships of elements. Applicants have amended claims 1 and 32, as discussed above, to further require that the elements are positioned in such manner that the electrophoretic medium separates the receptacle from the collection chamber. Applicants submit that a person of ordinary skill in the art would understand the language of the claims when read in light of the specification, and therefore, that the claims are definite.

For example, priority document USSN 60/121,836 indicates that the collection chamber can be physically contiguous with the electrophoretic medium, or it can interface with the electrophoretic medium by being in close proximity with the electrophoretic medium. The collection chamber can be detachable from the electrophoretic medium, allowing for the emptying or filling of the collection chamber and for the exchange of buffers. *See* the '836 application, page 4, lines 24-27. Thus, the receptacle and the collection chamber are physically separated from one another by the elctrophorectic medium, which forms a barrier between them. *See, e.g.*, the '836 application, page 6, line 29 through page 7, line 4; *see also* page 9, lines 14-20 of the instant specification.

Again, Figures 1, 2, and 4A of the specification are instructive as to the structural cooperative relationships between these elements, and one of ordinary skill in the art would recognize what is being claimed. Accordingly, this rejection should be withdrawn.

Rejections under 35 U.S.C. §102

Claims 1, 7-11, 32, 36 and 39 are rejected as anticipated by Weir *et al.*, Clinical Chemistry, 45(11):2047-2053 abstract #26 ("Weir"). The rejection is traversed.

The claims subject to the rejection are supported by priority document USSN 60/121,836, which was filed Feb. 26, 1999. Weir appears in an abstract of Poster Sessions associated with the

"San Diego Conference Nucleic Acid Technologies in Disease Detection November 17-19, 1999" (page 20 of Weir). Thus, Weir is not prior art to the claimed invention, and it is not available as a reference under 35 USC 102(a).

The Examiner has rejected claims 1, 7-11, 32, 36, and 39 under 35 U.S.C. § 102(f) in light of Weir. According to the Examiner, Weir names four individuals, of which three are co-inventors of the present application. Applicants respectfully submit that the Examiner's rejection of these claims for derivation is mistaken.

The present application names Lawrence W. Weir, Christopher P. Adams, T. Christian Boles, Rahul K. Dhanda, and Stephen J. Kron as co-inventors. The co-authors of Weir include Lawrence W. Weir, Christopher P. Adams, T. Christian Boles, and Rahul K. Dhanda. Thus, Dhanda is a co-author of Weir as well as a named co-inventor of the instant application. Although Weir can be considered as a reference with a different inventive entity because it does not name Stephen J. Kron as a co-author, it cannot be considered a reference that establishes prior conception of the claimed invention by another and communication of that conception to Applicants, as required to show derivation. *See* Price v. Symsek, 988 F.2d 1187, 1190 (Fed. Cir. 1993). As explained above, the '836 application was filed before the publication of Weir and teaches all of the relevant subject matter of claims 1, 7-11, 32, 36, and 39.

Thus, according to the evidence before the Examiner, the inventors of the instant application are the inventors of the instantly claimed invention. Applicants request that this rejection be withdrawn.

In view of the aforementioned remarks and amendments, the Applicants believe that each of pending claims is in condition for allowance. Reconsideration, withdrawal of the rejections, and passage of the case to issue is respectfully requested. A notice to this effect is earnestly solicited.

If, upon receipt and review of this amendment, the Examiner believes that the present application is not in condition for allowance and that changes can be suggested which would place the claims in allowable form, the Examiner is respectfully requested to call Applicant's undersigned counsel at the number provided below.

Respectfully submitted,

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